Analysis of laboratory parameters in patients with COVID-19: Experiences from a pandemic hospital

Laboratory parameters of COVID-19

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Abstract

Aim: This study aimed to determine the analysis of the laboratory parameters in patients infected with SARS-CoV-2 during the early pandemic period in Turkey. Material and Methods : This retrospective descriptive study was conducted at a pandemic hospital. All hospitalized patients and outpatients with a positive RT-PCR assay for SARS-CoV-2 were included in the study. Demographics, clinical characteristics, vital parameters on admission, laboratory findings, and drugs used for SARS-CoV-2 infection were obtained from the computer-based patient data system of the hospital and analyzed. The primary outcome of the study was the laboratory parameters of patients with COVID-19. The secondary outcome was 30-day all-cause mortality following emergency department admission.

Results: A total of 2,012 patients were included in study. The rates of hospitalization and 30-day mortality were 24% and 2%, respectively. The most common symptom was cough, and the most common comorbidity was hypertension. The neutrophil count, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio values were elevated in the non-survivor group compared to the survivor group (P = 0.001, P < 0.001, and P = 0.020, respectively). The lymphocyte and platelet counts were elevated in the survivor group compared to the non-survivor group (P = 0.001 and P < 0.001, respectively). As predictors of mortality, the cut-off value for the neutrophil, lymphocyte and platelet counts, and the neutrophil-to-lymphocyte and platelet-to-lymphocyte ratios were 5.68, 1.42, 195, 3.09, and 141.8, respectively, and the AUC was determined as 0.704, 0.714, 0.727, 0.745, and 0.610, respectively (P < 0.001, P < 0.001, P < 0.001, P < 0.001, and P = 0.023, respectively).

Discussion: The results of the study demonstrated that the neutrophil count, lymphocyte count, platelet count, neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio are useful in determining prognosis in SARS-CoV-2 infection.

Keywords

SARS-CoV-2; Clinical Characteristics; COVID-19; Mortality; Laboratory Parameters

Introduction

Coronaviruses are single-stranded, enveloped RNA viruses with positive polarity. Although they cause a self-limiting mild infection, which is common in society similar to the common cold, it can also lead to the development of more serious conditions, such as MERS-CoV and SARS-CoV infections [1]. In December 2019, a new type of coronavirus was reported to cause SARS and was named SARS-CoV-2. The respiratory syndrome caused by this virus was termed as coronavirus disease-2019 (COVID-19) [2]. After the emergence of the virus, by September 21, 2020, there have been over 31,000,000 SARS-CoV-2 cases, which were reported from 128 countries, and over 962,000 patients died as a result of this viral infection [3].

In Turkey, the first positive case of COVID-19 was identified on March 11, 2020, and the pandemic continues to spread increasingly [4]. There are many issues related to the COVID-19 disease that have not yet been clarified. In Turkey, there is a need for further research on the COVID-19 pandemic, which has negatively affected the whole world since December 2019. We considered that an analysis of laboratory parameters throughout Turkey might help predict the severity of the disease and clinical characteristics, given the rapid spread of SARS-CoV-2. Therefore, in this study, we aimed to determine the laboratory parameters of patients infected with SARS-CoV-2 during the early pandemic period in Turkey.

Material and Methods

Study design

This retrospective descriptive study was conducted at University of Health Sciences, Ümraniye Training and Research Hospital, a 672-bed tertiary academic hospital with an annual emergency department (ED) census of 438,000. We retrospectively collected the data of the patients who presented to our ED due to COVID-19-related symptoms between March 15, 2020 and April 15, 2020.

Study population

The study population comprised patients with suspected SARS-CoV-2 infection according to the COVID-19 Outbreak Management and Working Guidelines of the Turkish Ministry of Health (available at: https://covid19bilgi.saglik.gov.tr/tr/algoritmalar). Patients who met the criteria given in these guidelines were tested for SARS-CoV-2, and the diagnosis was made using the real-time reverse transcriptase-polymerase chain reaction (rt-PCR) test. Patients who did not undergo this test or tested negative for SARS-CoV-2 were excluded from the study. All hospitalized patients and outpatients with a positive RT-PCR assay for SARS-CoV-2 were included in the study. Decisions about the necessity of hospitalization were made by the emergency physician, or thoracic surgeon or cardiovascular surgeon in accordance with the same guidelines, independent of inpatient bed availability. Patients requiring hospitalization when no bed was available at our hospital were not transferred to other hospitals and waited in ED until a bed became available.

Data collection

Demographics, clinical characteristics (including travel to an endemic country, medical history, surgery history, exposure history, comorbidities, and symptoms), vital parameters on admission, laboratory findings, and drugs used for SARS-CoV-2 infection (hydroxychloroquine, favipiravir) were obtained from the computer-based patient data system of the hospital and analyzed by four independent researchers.

Comorbid diseases, such as chronic obstructive pulmonary diseases (COPD), diabetes mellitus (DM), hypertension, coronary artery disease (CAD), congestive heart failure (CHF), and active malignancy, chronic kidney disease (CKD), and immunosuppression. Symptoms including fever, cough, sputum, shortness of breath, weakness, muscle-joint pain, loss of taste or smell, headache, sore throat, nausea-vomiting, and diarrhea were recorded. Vital parameters were noted as blood pressure (systolic, and diastolic), heart rate, body temperature, respiratory rate, and oxygen saturation.

Laboratory parameters contained complete blood count [white blood cell count, lymphocyte count, neutrophil count, platelet count, hemoglobin count, hematocrit, mean platelet volume (MPV), mean corpuscular volume (MCV), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR)], renal and liver function, and measures of serum electrolytes, D-Dimer, C-reactive protein, troponin I, ferritin, and fibrinogen. Laboratory tests were conducted within 24 hours of hospital admission. The outcome within 24 hours of ED admission was recorded as discharged, admission to an inpatient clinic, admission to the intensive care unit (ICU), and death in ED. Contact history was defined as being in contact with a confirmed COVID-19 case or travelling to a country where the pandemic was seen within the last 14 days. The primary outcome of the study was the laboratory parameters of the patients with COVID-19, and the secondary outcome was 30-day all-cause mortality following ED admission.

Statistical analysis

IBM SPSS Statistics for Mac, Version 27.0. Armonk, NY, IBM Corp was used to perform statistical analyses. The Kolmogorov-Smirnov test was conducted to evaluate the conformity of variables to normal distribution. The data that matched normal distribution were presented with mean and standard deviation and values, and the remaining data were expressed as interquartile range and median values. Categorical data were presented with the number of cases and percentages. For the comparison of quantitative and qualitative data between two groups, the chi-square and Mann-Whitney U tests were used. We also formed a receiver-operating characteristic curve for 30-day mortality and obtained the area under the curve (AUC) for individual variables. The AUC values of the parameters were calculated and tested mutually for significance with the DeLong equality test. A p-value lower than 0.05 was considered statistically significant in all analyses.

Ethics

The ethical approval for our study was obtained from the Clinic Research Ethics Committee of University of Health Sciences, Ümraniye Training and Research Hospital (approval number: B.10.1.TKH.4.34.H.GP.0.01/97). We retrospectively reviewed the secondary data recorded from the computer-based patient data system of the hospital. The recorded data did not include any personally identifiable information and only contained clinical data; therefore, informed consent was waived.

Results

Among 20,077 patients presenting to our ED during the study period, 6,034 patients had symptoms of SARS-CoV-2 infection. A total of 2,012 patients with a positive RT-PCR assay result for SARS-CoV-2 were included in the final analysis. The study flowchart is given in Figure 1.

The mean age and standard deviation values of the 2,012 patients were 68.27 ± 13.02 years, and 1,166 patients (58%) were male. A total of 41 patients died within 30-day of ED admission. All deaths were in-hospital deaths and were due to COVID-19. The rates of hospitalization and 30-day mortality were 24% and 2%, respectively. Demographic characteristics, comorbid diseases, symptoms, vital parameters on admission, initial laboratory findings, and drugs used for SARS-CoV-2 infection are shown in Table 1-2.

Outcomes

Comparisons of characteristics of the non-survivor and survivor groups are shown in Table 1. Significant differences were detected between the survivor and non-survivor groups in terms of age (40.82 ± 14.3 versus 69.56 ± 12.81, P < 0.001), contact history (816 versus 32, P = 0.012), COPD (36 versus 4, P = 0.008), HT (178 versus 15, P < 0.001), CAD (36 versus 5, P = 0.001), CHF (9 versus 6, P < 0.001), CKD (10 versus 4, P < 0.001), active malignancy (16 versus 3, P = 0.006), cough (1286 versus 19, P = 0.012), sodium (138.94±2.49 versus 136.98 ± 5.82, P = 0.039), potassium (3.75 ± 18.22 versus 4.16 ± 1.08, P = 0.034), glucose [117 (64-355) versus 127 (78-519), P < 0.001], blood urea nitrogen (23.42 ± 14.05 versus 49.14 ± 32.87, P < 0.001), creatinine (0.79 ± 0.35 versus 1.4 ± 1.05, P = 0.001), albumin (4 ± 1.11 versus 3.5 ± 0.85, P = 0.007),

Table 1. Baseline characteristics of the enrolled patients and comparison of characteristics between the survivor and non-survivor groups

Variables	Total n = 2012 (%)	Survivor n = 1971 (%)	Non-survivor n = 41 (%)	p-value
Age, years	68.27 ± 13.02	40.82 ± 14.3	69.56 ± 12.81	<0.001
Gender				0.094
Male	1166 (58%)	1137 (57.7%)	29 (70.7%)	
Female	846 (42%)	834 (42.3%)	12 (29.3%)	
History of contact with a confirmed case				0.012
yes	1971 (98%)	816 (41.4%)	32 (78%)	
no	41 (2%)	1155 (58.6%)	9 (22%)	
History of travel to a country reporting COVID-19 cases				
yes	825 (41%)	11 (0.6%)	0	
no	1187 (59%)	1960 (99.4%)	41 (100%)	
Comorbidities (+%/-%)				
Chronic obstructive pulmonary diseases	40 (2%)	36 (1.8%)	4 (9.8%)	0.008
Hypertension	193 (9.6%)	178 (9%)	15 (36.6%)	<0.001
Diabetes mellitus	130 (6.5%)	126 (6.4%)	4 (9.8%)	0.334
Coronary artery disease	41 (2%)	36 (1.8%)	5 (12.2%)	0.001
Congestive heart failure	15 (0.7%)	9 (0.5%)	6 (14.6%)	<0.001
Chronic kidney disease	14(0.7%)	10 (0.5%)	4 (9.8%)	<0.001
Active malignancy	19 (0.9%)	16 (0.8%)	3 (7.3%)	0.006
Immunosuppression	4 (0.2%)	3 (0.2%)	1 (2.4%)	0.079
Hydroxychloroquine started in the first 24 hours	680 (33.8%)	677 (34.3%)	3 (7.3%)	<0.001
Favipiravir added to therapy	107 (5.3%)	75 (3.8%)	32 (78%)	<0.001
Intubation	27 (1.3%)	0	27 (65.9%)	
Symptoms				
Fever	673 (33.4%)	654 (33.2%)	19 (46.3%)	0.077
Cough	1305 (64.9%)	1286 (65.2%)	19 (46.3%)	0.012
Sputum	69 (3.4%)	68 (3.5%)	1 (2.4%)	0.725
Shortness of breath	654 (32.5%)	636 (32.3%)	18 (43.9%)	0.115
Weakness	287 (14.3%)	282 (14.3%)	5 (12.2%)	0.702
Muscle-joint pain	215 (10.7%)	211 (10.7%)	4 (9.8%)	0.846
Loss of taste or smell	75 (3.7%)	75 (3.8%)	0	0.402
Headache	132 (6.6%)	131 (6.6%)	1 (2.4%)	0.282
Sore throat	258 (12.8%)	254 (12.9%)	4 (9.8%)	0.553
Nausea-vomiting	71 (3.5%)	67 (3.4%)	4 (9.8%)	0.054
Diarrhea	91 (4.5%)	89 (4.5%)	2 (4.9%)	0.708
Vital parameters				
Systolic blood pressure	127.73 ± 24.11	121.85 ± 16.03	139.97 ± 27.99	0.001
Diastolic blood pressure	74.73 ± 9.71	74.45 ± 9.23	76.76 ± 13.33	0.336
Pulse pressure	90.18 ± 19.65	86.64 ± 16.48	97.48 ± 26.05	0.042
Body temperature	36.5 (35.9-39)	36.63 ± 0.63	37.02 ± 0.84	0.023
Respiratory rate	21 ± 4.35	19.09 ± 3.61	21.25 ± 5.75	0.158
Oxygen saturation	95 (70-98)	96 (76-99)	92 (70-96)	<0.001

Table 2. Laboratory parameters of the enrolled patients and comparison of them between the survivor and non-survivor groups

Variables	Total n = 2012 (%)	Survivor n = 1971 (%)	Non-survivor n = 41 (%)	p-value
pH	7.41 (7.02-7.46)	7.42 (7.01-7.55)	7.41 (7.13-7.51)	0.659
HCO3	24.71 ± 3.16	24.3 ± 6.7	22.16 ± 10.33	0.240
pCO2	36.5 ± 12.6	36.09 ± 13.87	36.36 ± 16.41	0.920
Lactate	95.5 (70-98)	1.3 ± 0.78	2 ± 1.81	0.027
Sodium, mEq/L	136.82 ± 3.71	138.94 ± 2.49	136.98 ± 5.82	0.039
Potassium, mmol/L	3.29 ± 1.94	3.75 ± 1.22	4.16 ± 1.08	0.034
Glucose, mg/dL	122 (78-355)	117 (64-355)	127 (78-519)	<0.001
Blood urea nitrogen, mg/dL	34.53 ± 27.9	23.42 ± 14.05	49.14 ± 32.87	<0.001
Creatinine, mg/dL	0.78 ± 0.42	0.79 ± 0.35	1.4 ± 1.05	0.001
Alanine aminotransferase, IU/L	18 (9-79)	22 (6-120)	23 (7-262)	0.278
Aspartate aminotransferase, IU/L	36 (8-76)	28 (8-159)	36 (15-454)	<0.001
D-Dimer, mg/L	2319.2 (26-16056.3)	125 (14-23817.2)	395 (26-8544.7)	0.086
Troponin (cTnI), ng/mL	0.09 (0.05-0.47)	0.05 (0.00-7.85)	0.32 (0.05-1.12)	<0.001
Ferritin, µg/l	373.02 ± 307.4	283.63 ± 354.13	1392.48 ± 1976.78	0.025
Fibrinogen, mg/dL	538.91 ± 134.7	469.16 ± 140.82	535.09 ± 155.69	0.038
C-Reactive Protein, mg/L	2.1 (0.2-21.7)	1.4 (0.1-21.7)	2.3 (0.2-24.6)	<0.001
White blood cell count	7.17 ± 5.11	7.48 ± 3.46	7.63 ± 4.90	0.843
Neutrophil count	7.50 ± 6.26	4.69 ± 2.74	7.29 ± 4.40	0.001
Lymphocyte count	1.06 ± 0.65	2.04 ± 1.08	1.44 ± 1.05	0.001
Platelet count	200.09 ± 48.69	241.60 ± 68.09	181.58 ± 66.5	<0.001
Hemoglobin count	11.09 (1.3-15.6)	13.2 (1.3-16.8)	13.3 (1.10-17.3)	0.027
Hematocrit count	34.2 (4.1-44.8)	39.5 (3.9-48.9)	39.2 (3.9-52.1)	0.007
Mean platelet volume	10.04 ± 1.17	8.83 ± 2.76	9.73 ± 2.36	0.037
Mean corpuscular volume	85.01 ± 6.61	78.54 ± 23.01	81.54 ± 21.25	0.408
Neutrophil-to-lymphocyte ratio	5.77 (0.03-57.3)	3.32 (0.04-53.14)	6.09 (0.03-57.32)	<0.001
Platelet-to-lymphocyte ratio	185.95 (78.9-876.1)	147.7 (53.6-1357.1)	164.1 (31.7-510.81	0.020

Table 3. Ability of the investigated laboratory parameters to predict 30-day all-cause mortality following ED admission

	AUC	Cut-off	Sensitivity	Specificity	PPV	NPV	Accuracy	95% CI	p-value
Neutrophils	70.4	>5.68	63.4	71.3	4.7	98.9	34.7	68.3-78.4	<0.001
Lymphocytes	71.4	≤1,42	73.6	71.5	5.1	99.2	45.2	69.6-73.7	<0.001
Platelets	72.7	≤195	60.9	74.6	5.0	98.9	35.5	70.6-74.7	<0.001
NLR	74.5	>3.09	81.5	70.1	5.4	99.5	51.	72.4-76.4	<0.001
PLR	61.0	>141.8	63.1	66	3.7	98.9	29.2	58.7-63.2	0.023
MPV	61.8	>9.4	68.2	50.1	2.9	98.6	18.4	59.6-64.0	0.012

AUC: Area under curve; PPV: positive predictive value; CI: confidence interval; NPV: Negative predictive value; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; MPV: mean platelet volume
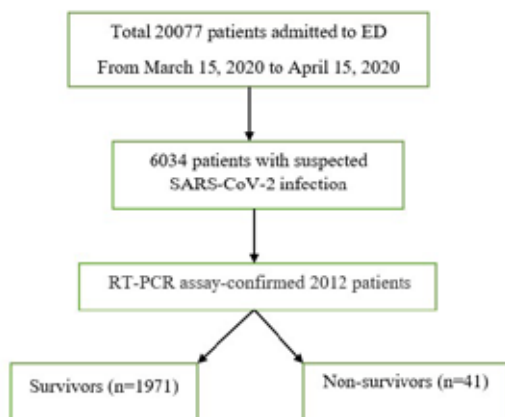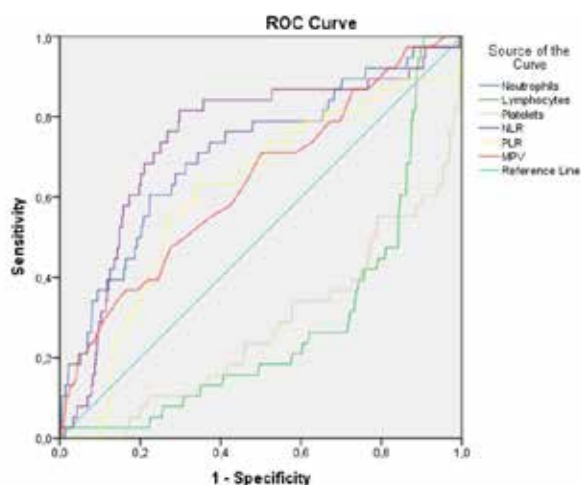

Figure 1. Flowchart of the study

Figure 2. The ROC curve predicting the 30-day all-cause mortality after ED admission

aspartate aminotransferase [28 (8-159) versus 36 (15-454), P < 0.001], troponin [0.05 (0.00-7.85) versus 0.32 (0.05-1.12), P < 0.001], fibrinogen (469.16 ± 140.82 versus 535.09 ± 155.69), P = 0.038], and CRP [1.4 (0.1-21.7) versus 2.3 (0.2-24.6), P < 0.001]. Significant differences were also identified between the survivor and non-survivor groups in relation to the hematological test parameters: neutrophil count (4.69 ± 2.74 versus 7.29 ± 4.40, P = 0.001), lymphocyte count (2.04 ± 1.08 versus 1.44 ± 1.05, P = 0.001), platelet count (241.60 ± 68.09 versus 181.58 ± 66.5, P < 0.001), hemoglobin count [13.2 (1.3-16.8) versus 13.3 (1.10-17.3), P = 0.027], hematocrit [39.5 (3.9-48.9) versus 39.2 (3.9-52.1), P = 0.007)], MPV (8.83±2.76 versus 9.73±2.36, P = 0.037), NLR [3.32 (0.04-53.14) versus 6.09 (0.03-57.32), P < 0.001], and PLR [147.7 (53.6-1357.1) versus 164.1 (31.7-510.81), P = 0.020].

Table 3 and Figure 2 present the cut-off, sensitivity and specificity and AUC values with a 95% confidence interval of the investigated parameters.

Discussion

In this study, we performed a comprehensive evaluation of 2,012 adult patients with SARS-CoV-2 infection at a pandemic hospital in Turkey to contribute to the limited data on SARS-CoV-2 cases in the country. All the patients in this study were confirmed to have SARS-CoV-2 based on a positive RT-PCR assay.

Some studies have identified an association between the severity of COVID-19 and low lymphocyte count. The literature contains the hypotheses of the possible underlying pathogenesis concerning COVID-19-induced lymphopenia [5-9]. Mazzoni et al. suggested that the massive lymphocyte death that occurred due to an inflammatory cytokine storm might be a possible underlying cause of lymphopenia [6]. In an in vitro study, Xiong et al. showed that SARS-CoV-2 could infect T cells [7]. Ouyong et al. reported that in severe COVID-19 patients, T cell activation and functions were affected by the downregulation of MAP2K7 and SOS1, which, they hypothesized, could be a result of cytokine storm [8]. In another study, Dialo et al. showed an increase in some apoptosis proteins of T cells, such as PD-1 and Tim-3; thus, they suggested that the exhaustion of T cells could be involved in the pathogenesis of lymphopenia [9].

NLR has been investigated as an independent prognostic marker in critically ill patients, as well as in those with severe sepsis, septic shock, and other diseases [10-12]. Yang et al. reported that NLR and PLR might be related to the severity of infection in patients with SARS-CoV-2 [11]. In that study, the cut-off values for NLR and PLR as predictors of severity were determined as 3.3 and 180, respectively in patients with SARS-CoV-2 infection, and their AUC values were 0.743 and 0.784, respectively [11]. In a meta-analysis conducted by Chan et al. examining a total of 20 studies and 3,508 patients, NLR and PLR were suggested to be independent biologic prognostic markers of the severity of SARS-CoV-2 infection [12]. In that study, elevated NLR and PLR values were associated with severe disease (standard mean difference: 2.80 and 1.82; 95% confidence interval: 2.12-3.48 and 1.03- 2.61, respectively; P < 0. 01 for both) [12]. Similarly, the results of the current study showed that NLR and PLR were elevated in the non-survivor

group compared to the survivor group.

In recent studies, it was demonstrated that thrombocytopenia might be an indicator of poor outcome and worsening illness [13-16]. Our findings are consistent with those of previous studies. In the literature, several mechanisms have been proposed to explain the pathogenesis of thrombocytopenia. As in other coronavirus infections, SARS-CoV-2 may reduce platelet production by infecting bone marrow cells and abnormal hematopoiesis [14]. Mehta et al. showed that cytokine storm reduces the bone marrow's ability to make new blood cells, and destroy the hematopoietic progenitor cells, in SARS-CoV-2 infected patients [15]. Xu et al. speculated that the increasing level of immune complexes and autoantibodies could cause immune-mediated thrombocytopenia. SARS-CoV-2 infection causes damage to pulmonary endothelial cells and lung tissues. Endothelial damage results in platelet activation and micro embolisms [16]. Another hypothesis about thrombocytopenia in SARS-CoV-2-infected patients is an increase in platelet consumption due to the formation of microthrombi, and aggregation of platelets [16].

Limitations

The main limitation of this study is its retrospective nature. Secondly, our study was conducted in a single center with an observational design, and therefore the results may not be generalizable to other healthcare institutions. Thirdly, in our study, the survivor and non-survivor groups were not similar in terms of age and gender. In addition, as factors that may have an impact on laboratory parameters, physical activity, alcohol consumption, and BMI, may have led to potential bias. Less biased results can be obtained with prospective studies.

Conclusion

The results of this study demonstrated that the neutrophil count, lymphocyte count, platelet count, NLR, PLR and MPV are useful in determining prognosis in SARS-CoV-2 infection. These laboratory parameters can be used as an indicator to help prevent and control the COVID-19 pandemic.

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